

POLYPEPTIDE COMPOSITIONS

- [0067] Novel sulfatases, as well as polypeptide compositions related thereto, are provided. The invention provides a sulfatase present in other than its natural environment. Novel sulfatases of the invention encompass SULF1 and SULF2. In some embodiments, a subject sulfatase is a human sulfatase. In other embodiments, a subject sulfatase is a mouse sulfatase.
- [0068] In particular embodiments, a subject sulfatase has an amino acid sequence substantially identical to the sequence of any one of SEQ ID NOS:03, 06, 09, 12, 15, and 18. In other particular embodiments, a subject sulfatase has an amino acid sequence substantially identical to any one of the sequences depicted in Figure 1B, Figure 2B, Figure 3B, Figure 4B, Figure 10B, and Figure 11B.
- [0069] In many embodiments, a novel sulfatase of the invention exhibits one or more of the following properties: (1) exhibits glucosamine-6-sulfatase activity; (2) is an endosulfatase, removing sulfate from the C-6 position of internal glucosamines as well as from glucosamines at the non-reducing termini of polysaccharides (3) removes a sulfate group from glycoproteins and/or proteoglycans; (4) is secreted from a eukaryotic cell; (5) acts on extracellular matrix (ECM) components to remove a sulfate group, resulting in release from the ECM of extracellular differentiation factors and/or growth factors; (6) mRNA encoding the sulfatase shows elevated expression in tumors; and (7) is secreted in greater abundance from a cancerous cell as compared to a non-cancerous cell of the same cell and/or tissue type.
- [0070] The invention also provides fragments of the subject sulfatases. In some embodiments, fragments exhibit sulfatase activity. Fragments find utility in generating antibodies to the full-length sulfatases; and in methods of screening for candidate agents that bind to and/or modulate sulfatase enzymatic activity. The term "sulfatase polypeptide composition" as used herein refers to both the full-length human protein as well as portions or fragments thereof. Also included in this term are variations of the naturally occurring human protein, where such variations are homologous or substantially similar to the naturally occurring protein, as described in greater detail below, as well as corresponding homologs from non-human species, such as other mammalian species. In the following description of the subject invention, the terms

"SULF1" and "SULF2" are used to refer not only to the human form of these novel sulfatases, but also to homologs thereof expressed in non-human species.

[0071] Human SULF1 (huSULF1) is an 871 amino acid protein having an amino acid sequence as shown in Fig. 1B and identified as SEQ ID NO:03. HuSULF1 has a molecular weight based on its amino acid of about 80 to about 100 kDa.

[0072] Human SULF2 (huSULF2) is an 870 amino acid protein having an amino acid sequence as shown in Fig. 2B and identified as SEQ ID NO:06. HuSULF2 has a molecular weight based on its amino acid of about 80 to about 100 kDa. In some embodiments, a subject sulfatase has an amino acid sequence as shown in Figure 10B and as set forth in SEQ ID NO:15.

[0073] Mouse SULF1 (mSULF1) is an 870 amino acid protein having an amino acid sequence as shown in Figure 3B and as set forth in SEQ ID NO:09.

[0074] Mouse SULF2 (mSULF2) is an 875 amino acid protein having an amino acid sequence as shown in Figure 4B and as set forth in SEQ ID NO:12. In some embodiments, a subject sulfatase has an amino acid sequence as shown in Figure 11B and as set forth in SEQ ID NO:18.

[0075] The subject sulfatases have a molecular weight of between 80 and 100 kDa based on their amino acid sequences. Subject sulfatases produced by a eukaryotic cell are glycosylated, and in some embodiments have a molecular weight of about 126 kDa. In addition, in some embodiments, a subject sulfatase is proteolytically cleaved to produce fragments of from about 60 kDa to about 70 kDa (e.g., 61 kDa, 66 kDa, 71 kDa); from about 48 kDa to about 55 kDa (e.g., 49 kDa, 53 kDa); or from about 40 to about 55 kDa (e.g., 40 kDa, 49 kDa, 53 kDa). Many of these fragments or associations of these fragments have sulfatase activity.

[0076] In addition to the above specifically listed proteins, sulfatases from other species are also provided, including mammals, such as: rodents, e.g. mice, rats; domestic animals, e.g. horse, cow, dog, cat; and humans, as well as non-mammalian species, e.g. avian, and the like. By homolog is meant a protein having at least about 35 %, at least about 40%, at least about 60 %, at least about 70%, at least about 75%, at least about 80%, at least about 90%, or at least about 95%, or higher, amino acid sequence identity to the one of the above specifically listed sulfatases, as measured by using the "GAP" program (part of the Wisconsin Sequence Analysis Package available through the